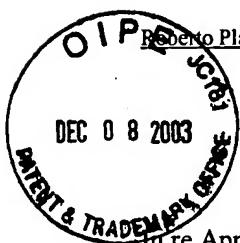


**CERTIFICATE OF MAILING**

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Roberto Plascencia Roberto Pla

**PATENT**

**Attorney Docket No. 25352-0033 D1**

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Application	)	<b>PATENT APPLICATION</b>
Inventor(s): Edgardo Laborde et al.	)	Art Unit: Not Assigned
Application No.: 10/716,652	)	Examiner: Not Assigned
Filed: 11/18/2003	)	
Title: Antagonists of MCP-1 Function and Methods of Use Thereof	)	

**INFORMATION DISCLOSURE STATEMENT UNDER 37 C.F.R. §1.97**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313

Sir:

Listed below or on an attached Form PTO-1449 is information known to applicant(s). A copy of each listed publication and U.S. and foreign patent, along with a concise explanation of information in a foreign language, if any, except for pending U.S. applications is attached or is identified with an asterisk as having been previously cited in priority U.S. Patent Application No.: 10/106,881, filed: 03/25/2002, pursuant to 37 C.F.R. §1.97-1.98.

*1.98(d) A copy of any patent, publication or other information listed in an information disclosure statement is not required to be provided if it was previously cited by or submitted to the office in a prior application, provided that the prior application is properly identified in the statement and relied upon for an earlier filing date under 35 U.S.C. 120.*

Applicants respectfully request that the listed information be considered by the Examiner and be made of record in the above-identified application. If form PTO-1449 is enclosed, the Examiner is requested to initial and return it in accordance with MPEP §609.

This statement is not intended to represent that a search has been made or that the information cited in the statement is, or is considered to be, material to patentability as defined in §1.56.

- This statement qualifies under 37 C.F.R. §1.97, subsection (b) because (check all that apply):
- (1) It is being filed within 3 months of the application filing date and is other than a continued prosecution application under § 1.53(d)  
-- OR --
- (2) It is being filed within 3 months of entry of a national stage  
-- OR --
- (3) It is being filed before the mail date of the first Office Action on the merits  
-- OR --
- (4) It is being filed before the mailing of a first Office Action after the filing of a request for continued examination under § 1.114.
- 37 C.F.R. §1.97(c). If this statement is being filed after the latest of: (1) three months beyond the filing date of a national application; (2) three months beyond the date of entry of the national stage as set forth in §1.491 in an international application; or (3) the mailing date of a first Office action on the merits, but before the mailing date of the earlier of a final office action under §1.113 or a notice of allowance under §1.311, then:
- a certification as specified in §1.97(e) is provided below; or
- a fee of \$180.00 as set forth in §1.17(p) is authorized below, enclosed, or included with the payment of other papers filed together with this statement.
- 37 C.F.R. §1.97(d). If this statement is being filed after the mailing date of the earlier of a final office action under §1.113 or a notice of allowance under §1.311, but before payment of the issue fee, then:
- A. a certification as specified in §1.97(e) is completed below; and
- B. a petition under 37 C.F.R. §1.97(d) requesting consideration of this statement is submitted herewith; and
- C. a fee of \$130.00 as set forth in §1.17(i)(1) is authorized below, enclosed, or included with the payment of other papers filed together with this statement.
- Fee Authorization. The Commissioner is hereby authorized to charge the above-referenced fees of \$0.00 and charge any additional fees or credit any overpayment associated with this communication to Deposit Account No. 08-1641 (Docket No. 25352-0033 D1).

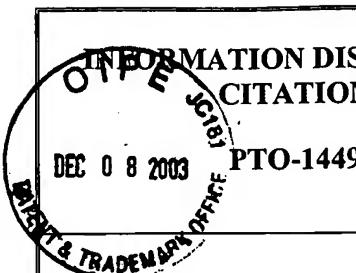
Respectfully submitted,

HELLER EHRLMAN WHITE & MCAULIFFE LLP

Dated: December 4, 2003

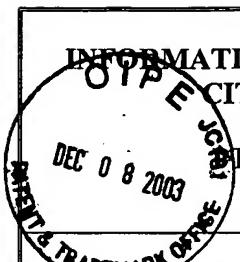
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Customer No. 25213

 <b>INFORMATION DISCLOSURE CITATION</b> DEC 08 2003 PTO-1449		ATTY. DOCKET NO. 25352-0033 D1		SERIAL NO. 10/716,652		
		APPLICANT Edgardo Laborde et al.				
		FILING DATE 11/18/2003			GROUP Not Assigned	
		<b>U.S. PATENT DOCUMENTS</b>				
EXAMINER'S INITIALS	PATENT NO.	DATE	NAME	CLASS	SUBCLASS	FILING DATE
	* 3,823,144	07/09/1974	Schmitt et al.	544	377	06/21/1972
	* 4,269,990	05/26/1981	May et al.	548	315	12/05/1979
	* 5,977,108	11/02/1999	Kikuchi et al.	514	249	06/27/1996
	* 6,140,338	10/2000	Naya et al	514	299	
<b>FOREIGN PATENT DOCUMENTS</b>						
EXAMINER'S INITIALS	PATENT NO.	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION
						YES
	* 2 001 284	09/26/2969	FR	A 61 K	21/00	
	* 1 250 611	10/28/1974	GB	C07D	99/22	
	* 9-255572	09/1997	Japan			
	00/46198	08/2000	PCT			
	* 01/57021	08/09/2001	PCT	C07D	401/14	
	* 01/57003	08/09/2001	PCT	C07D	265/36	
	* 01/57044	08/2001	PCT			
	* 92/14710	09/03/1992	PCT	C07D	211/26	
	* 97/24325	07/1997	PCT			
<b>OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)</b>						
	* Alam et al., "Increased MCP-1, RANTES, and MIP-1 $\alpha$ in Bronchoalveolar Lavage Fluid of Allergic Asthmatic Patients", <i>Am J Respir Crit Care Med</i> , 153:1398-1404. (1996)					
	* Alcami et al., "Blockade of Chemokine Activity by a Soluble Chemokine Binding Protein form Vaccinia Virus", <i>J Immunol</i> , 160:624-633 (1998)					
	* Antoniades et al., "Expression of monocyte chemoattractant protein 1 mRNA in human idiopathic pulmonary fibrosis", <i>Proc Natl Acad Sci USA</i> , 89:5371-5375 (1992)					
	* Ajuebor et al., " Endogenous monocyte chemoattractant protein-1 recruits monocytes in the zymosan peritonitis model", <i>Journal of Leukocyte Biology</i> , vol. 63:108-116, January 1998					
	* Baggolini et al., "Human Chemokines; an update", <i>Annu rev Immunol</i> (1997), pp. 15:675-705					
	* Baggolini, "Chemokines and Leukocyte Traffic, <i>Nature</i> vol: 392:9 pp 565-568, (1998)					
EXAMINER		DATE CONSIDERED				

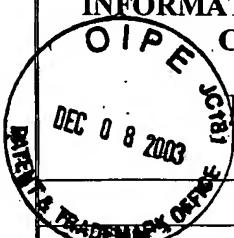
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If an asterisk is placed beside the reference number, a copy is not provided because the reference was previously cited by or submitted to the PTO in a prior application that is identified in the statement and relied upon for an earlier filing date under 35 U.S.C. 120, 37 C.F.R. 1.98(d).

 <b>INFORMATION DISCLOSURE STATEMENT</b> <b>TO-1449</b>		ATTY. DOCKET NO. 25352-0033 D1		SERIAL NO. 10/716,652		
		APPLICANT Edgardo Laborde et al.				
		FILING DATE 11/18/2003		GROUP Not Assigned		
<b>U.S. PATENT DOCUMENTS</b>						
EXAMINER'S INITIALS	PATENT NO.	DATE	NAME	CLASS	SUBCLASS	FILING DATE
	* 6,288,103	09/2001	Faull et al	514	419	
	* 6,316,449	11/2001	Bratton et al.	514	252.04	
	* 6,329,402	12/11/2001	Kikuchi et al.	514	341	05/17/1999
	* 6,342,516	01/2002	Umeda et al.	514	397	
<b>FOREIGN PATENT DOCUMENTS</b>						
EXAMINER'S INITIALS	PATENT NO.	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION
						YES
	* 97/44329	11/1997	PCT			
	* 98/02151	01/1998	PCT			
	* 98/04554	05/1999	PCT			
	* 98/06703	02/1998	PCT			
	* 98/27815	07/1998	PCT			
	* 99/40072	08/12/1999	PCT	C07D	235/16	
<b>OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)</b>						
	* Boring et al., "Decreased lesion formation in CCR2 <sup>-/-</sup> mice reveals a role for chemokines in the initiation of atherosclerosis", <i>Nature</i> , 394:894-897 (1998)					
	* Bright et al., "Identification of a Non Peptidic Rantes Antagonist", <i>Bioorg Med Chem Lett</i> , 8:771-774 (1998)					
	* Campbell et al., "Monocyte Chemoattractant Protein-1 Mediates Cockroach Allergen-Induced Bronchial Hyperreactivity in Normal but Not CCR2 <sup>-/-</sup> Mice: The Role of Mast Cells", <i>J Immunol</i> , 163:2160-2167 (1999)					
	Chemical Abstracts, 103(17), Abst. No. 141873u (1985); Abstract of Kuzzinski, L. et al: "Synthesis of new 4 and 5 disubstituted isothiazoles "Pol J Pharmacol Pahrm, 36(5):485-491 (1984)					
	Chemical Abstracts, 100(21), Abst. No. 174751u (1984): Abstract of Ormek, G. et al., "Ring-opening reactions of potentially biologically active benzothienooxazines" Arc Pharm, 317(2):117-120 (1984)					
	* Folkman and Shing, "Control of Angiogenesis by Heparin and Other Sulfated Polysaccharides", <i>Adv Exp Med Biol.</i> , 313:355-364 (1992)					
	* Forbes et al., "CCR2B Receptor Antagonists: Conversion of a Weak HTS Hit to a Potent Lead Compound", <i>Bioorg Med Chem. Lett</i> , 10:1803-1806 (2000)					
EXAMINER	DATE CONSIDERED					

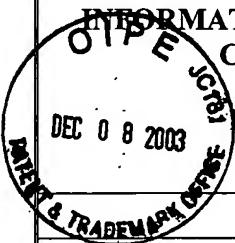
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<b>INFORMATION DISCLOSURE CITATION</b>  <b>PTO-1449</b>		ATTY. DOCKET NO. 25352-0033 D1	SERIAL NO. 10/716,652
		APPLICANT Edgardo Laborde et al.	
		FILING DATE 11/18/2003	GROUP Not Assigned
		<b>OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)</b>	
<ul style="list-style-type: none"> <li>* Gosling et al., "MCP-1 deficiency reduces susceptibility to atherosclerosis in mice that over express human apo37lipoprotein B", <i>J Clin Invest</i>, 103:773-778 (1999)</li> </ul>			
<ul style="list-style-type: none"> <li>* Gu et al., "Absence of Monocyte Chemoattractant Protein-1 Reduces Atherosclerosis in Low Density Lipoprotein Receptor-Deficient Mice", <i>Mol Cell</i>, 2:275-281 (1998)</li> </ul>			
<ul style="list-style-type: none"> <li>* Hesselgesser, "Identification and Characterization of Small Molecule Functional Antagonists of the CCR1 Chemokine Receptor", <i>J. Biol Chem</i>, 273:15687-15692 (1998)</li> </ul>			
<ul style="list-style-type: none"> <li>* Hoogewerf et al., "Glycosaminoglycans Mediate Cell Surface Oligomerization of Chemokines", <i>Biochemistry</i> 36:13570-13578, (1997).</li> </ul>			
<ul style="list-style-type: none"> <li>* Hosaka et al., "Expression of the Chemokine Superfamily in Rheumatoid Arthritis", <i>Clin Exp Immunol</i>, 97:451-457. (1994)</li> </ul>			
<ul style="list-style-type: none"> <li>* Hsieh et al., "Immunotherapy Suppresses the Production of monocyte chemotactic and activating factor and augments the production of IL-8 in Children with Asthma", <i>J Allergy Clin Immunol</i>, 98:580-587 (1996)</li> </ul>			
<ul style="list-style-type: none"> <li>* Kitano M. et al., "Synthesis and Biological Activity of N-(Aminoiminomethyl)-1H-Idoleca Rboxamide Inhibitors", <i>Chem and Pharm Bulletin, Pharmaceutical Society of Japan</i>, vol. 47, no. 11, 11/1999, pp 1538.</li> </ul>			
<ul style="list-style-type: none"> <li>* Koch et al., "Enhanced Production of Monocyte Chemoattractant Protein-1 in Rheumatoid Arthritis", <i>J Clin Invest</i>, 90:772-779, (1992)</li> </ul>			
<ul style="list-style-type: none"> <li>* Kunkel et al., "The Role of Chemokines in Inflammatory Joint Disease", <i>J Leukocyte Biol</i>, 59:6-12 (1996)</li> </ul>			
<ul style="list-style-type: none"> <li>* Kurashima et al., "Increase of Chemokine Levels in Sputum Precedes Exacerbation of Acute Asthma Attacks", <i>J Leukocyte Biol</i>, 59:313-316, (1996)</li> </ul>			
<ul style="list-style-type: none"> <li>* Kuschert et al., "Glycosamineoglycans interact selectively with chemokines and modulate receptor binding and cellular responses", <i>Biochemistry</i> 38:12959-12968, (1999).</li> </ul>			
<ul style="list-style-type: none"> <li>* Liang et al., "Identification and characterization of a potent, selective and orally active antagonist of the cc chemokine receptor-1", <i>The Journal of Biological Chemistry</i>, vol. 25:19000-19008, June 23, 2000.</li> </ul>			
<ul style="list-style-type: none"> <li>* Luster, "Chemokines_Chemotactic Cytokines That Mediate Inflammation", <i>The New England Journal of Medicine</i>, pp. 436-445, February 12, 1998</li> </ul>			
<ul style="list-style-type: none"> <li>* McFadden and Kelvin, "New Strategies for Chemokine Inhibition and Modulation", <i>Biochem Pharmacol</i>, 54:1271-1280 (1997)</li> </ul>			
<ul style="list-style-type: none"> <li>* Mirzadegan et al., "Identification of the binding site for a novel class of CCR2bcemokine receptor antagonists...", The American Society for Biochemistry and Molecular Biology, Inc., manuscript M000692200, (2000).</li> </ul>			
<ul style="list-style-type: none"> <li>* Moore et al., "Tumor angiogenesis is regulated by CXC chemokines", <i>J Lab Clin Med</i>, 132:97-103 (1998)</li> </ul>			
<ul style="list-style-type: none"> <li>* Moore et al., "CXC Chemokine Modulation of angiogenesis...", <i>J Investigative Medicine</i>, vol 46:113-120 (1998)</li> </ul>			
EXAMINER	DATE CONSIDERED		

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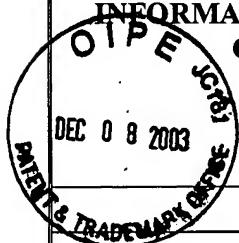
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	25352-0033 D1	10/716,652
	APPLICANT Edgardo Laborde et al.	
	FILING DATE 11/18/2003	GROUP Not Assigned
<b>OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)</b>		
* Murphy, "The Molecular Biology of Leukocyte Chemoattractant Receptors", <i>Annu Rev Immunol</i> , 12:593-633, (1994)		
* Nelken et al., "Monocyte Chemoattractant Protein-1 in Human Atheromatous Plaques", <i>J. Clin Invest</i> , 88:1121-1127 (1991)		
* Okada et al., "Synthesis and Antitumor Activities of Water-Soluble Benzoylphenylureas", <i>Chem Pharm Bull</i> , 47:430-433, (1999)		
* Okada et al., "Synthesis and Antitumor Activities of Prodrugs of Benzoylphenylureas", <i>Chem Pharm Bull</i> 42:57-61, (1994)		
* Okada et al., "Synthesis and Antitumor Activities of Novel Benzoylphenylurea Derivatives", <i>Chem Pharm Bull</i> , 39:2308-2315 (1991)		
* Proost et al., "The Role of Chemokines in Inflammation", <i>Int J Clin Lab Res</i> , 26:211-223, (1996)		
* Robinson et al., "Chemokine expression in Rheumatoid Arthritis...", <i>Clin Exp Immunol</i> 101:398-407 (1995)		
* Rollins, "Chemokines", <i>Blood</i> , vol 90 no. 3, pp. 909-928, August 1, 1997		
* Rousseau, Jean-Francois et al., Chemical Abstract, "Regioselective ortho-directed metalation and electrophilic substitution of indole and indoling -5-(N-phenyl) carboxamides" retrieved from STN database accession no. 136:355126 XP002206081 abstract & Heterocycles 92001), 55(12), 2289-2304		
* Rovin et al., "Chemotactic Factors and Renal Inflammation", <i>American Journal of Kidney Diseases</i> , 31:1065-1084, June 1998		
* Rovin, "Chemokines as Therapeutic Targets in Renal Inflammation", <i>American Journal of Kidney Diseases</i> , 34: 761-767, October 1999		
* Rovin, "Chemokine blockade as a therapy for renal disease", <i>Current Opinion in Nephrology and Hypertension</i> , 13:225-232, (2000)		
* Rovin et al., "A Novel Polymorphism in the MCP-1 Gene Regulatory Region That Influences MCP-1 Expression", <i>Biochemical and Biophysical Research Communications</i> , 259, pp. 344-348, (1999)		
* Saunders and Tarby, "Opportunities for novel therapeutic agents acting at chemokine receptors", <i>Drug Discovery Today</i> , vol. 4 No. 2 (1999)		
* Schall, "Biology of the RANTES/SIS Cytokine Family", <i>Cytokine</i> , 3:165-183, (1991)		
* Sendo et al., "Regulation of leukocyte adherence and migration by glycosylphosphatidyl-inositol-anchored proteins", <i>Journal of Leukocyte Biology</i> , vol. 66, pp. 369-374, September 1999		
* Servant et al., "Polarization of Chemoattract Receptor Signaling During Neutrophil Chemotaxis", <i>Science</i> , vol. 287: 1037-1040, February 11, 2000		
* Strieter et al., "The Immunopathology of Chemotactic Cytokines: The Role of Interleukin-8 and Monocyte Chemoattractant Protein-1", <i>J Lab Clin Med</i> , 123:183-197 (1994)		
* Sugiyama et al., "Chemokines in Bronchoalveolar Lavage Fluid in Summer-type Hypersensitivity Pneumonitis", <i>Eur Respir J</i> , 8:1084-1090 (1995)		
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SHEET 5 OF 5

<p style="text-align: center;"><b>INFORMATION DISCLOSURE CITATION</b> <b>PTO-1449</b>  </p>	ATTY. DOCKET NO. 25352-0033 D1	SERIAL NO. 10/716,652
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*	Szekanecz et al., "Cytokines in Rheumatoid Arthritis", <i>Drugs and Aging</i> , 12:377-390, May 12, 1998	
*	Taub, D.D. "Chemokine-Leukocyte Interactions", <i>Cytokine Growth Factor Rev</i> , 7:355-376, (1996)	
*	Takeya et al., "Detection of Monocyte Chemoattractant Protein-1 in Human Atherosclerotic Lesions by an Anti-monocyte Chemoattractant Protein-1 Monoclonal Antibody", <i>Human Pathol</i> , 24:534-539 (1993)	
*	Tanaka et al., "T-cell adhesion induced by proteoglycan-immobilized cytokine MIP-1 $\beta$ ", <i>Nature</i> , 361:79-82 (1993)	
*	Trivedi et al., "Chemokines: Targets for novel therapeutics", <i>Annual Reports in Medicinal Chemistry</i> , 35:191-200, (2000)	
*	Vaddi and Newton, "Comparison of biological responses of human monocytes and THP-1 cells to chemokines from the intercrine- $\beta$ family", <i>Journal of Leukocyte Biology</i> , vol 55: 756-761, June 1994	
*	Villiger et al., "Production of Monocyte Chemoattractant Protein-1 By Inflamed Synovial Tissue and Cultured Synoviocytes", <i>J Immunol</i> , vol. 149, pp. 722-727, (1992)	
*	Vlodavsky et al., "Involvement of heparan sulfate and related molecules in sequestration and growth promoting activity of fibroblast growth factor", <i>Cancer and Metastasis Reviews</i> 15: 177-186, (1996)	
*	Waltenberger et al., "Suramin is a Potent Inhibitor of Vascular Endothelial Growth Factor. A Contribution to the Molecular Basis of its Antiangiogenic Action", <i>J Mol Cell Cardiol</i> , 28:1523-1529, (1996)	
*	Wang et al., "Chemokines and their role in tumor growth and metastasis", <i>Journal of Immunological Methods</i> , 220: 1-17, (1998)	
*	Wellstein and Czubayko, "Inhibition of fibroblast growth factors", <i>Breast Cancer Res Treat</i> , 38:109-119 (1996)	
*	White, "Identification of a Potent, Selective Non-peptide CXCR2 Antagonist That Inhibits Interleukin-8-induced Neutrophil Migration", <i>J. Bio Chem</i> , 273:10095-10098 (1998)	
*	Wrenshall et al., "Modulation of macrophage and B cell function by glycosaminoglycans", <i>Journal of Leukocyte Biology</i> , vol. 66:391-400, September 1999	
*	Yang et al., "Fully human anti-interleukin-8 monoclonal antibodies: potential therapeutics for the treatment of inflammatory disease states", <i>Journal of Leukocyte Biology</i> , vol. 66: 401-410, September 1999	
*	Yla-Herttula et al., "Expression of Monocyte Chemoattractant Protein 1 in Macrophage-Rich Areas of Human and Rabbit Atherosclerotic Lesions", <i>Proc Natl Acad Sci USA</i> , 88:5252-5256 (1991)	
*	Zetsche et al., Crossfire Beilstein 'Online' Beilstein Institut für Förderung der Wissenschaften, Frankfurt, DE; Abstract, <i>Chemische Berichte</i> , vol. 72, 1939, page 1599	
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